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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/603,501	06/24/2003	Nicholas Franano	55225 CON (47703)	3974

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EDWARDS & ANGELL, LLP
P.O. BOX 55874
BOSTON, MA 02205

EXAMINER	
AFREMOVA, VERA	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 12/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/603,501	FRANANO, NICHOLAS	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25 and 40-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25 and 40-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of the group III (original claims 12, 25-33 and 35) in the reply filed on 9/30/2005 is acknowledged. The traversal is on the ground(s) that original groups III and IV (both drawn to *in vivo* applications of therapeutic agent) are not distinct since they differ in a mere recitation of various disorders related to obstruction of biological conduit(s). This is not found persuasive because various disorders would clearly require different protocols of treatments and the references that would be applied to one method would not necessarily anticipate or render obvious the other method. Moreover, as to the question of burden of search, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Burden in examining materially different groups having materially different issues also exists. For these reasons, the restriction requirement is deemed proper and is adhered to and made final.

In response to election/restriction applicant canceled all non-elected claims (drawn to *in vitro* applications and kit with therapeutic agents and materials) and presented claim amendment changing scope of the claimed invention.

Claims 25 as amended and new claims 40-54 are pending and under examination.

Claim Rejections - 35 USC §112

New matter

Claims 25 as amended and new claims 40-54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Insertion of the limitation drawn to administering "elastase in a dose sufficient to cause enlargement of the diameter of artery or vein" in the method for *in vivo* application of therapeutic composition has no support in the as-filed specification. The insertion of this limitation is a new concept because it neither has literal support in the as-filed specification by way of generic disclosure, nor are there specific examples of the newly limited genus that would show possession of the concept of the use of "elastase in a dose sufficient to cause enlargement of the diameter of artery or vein" including applications to human patients, including treating artery or vein obstructed by stenosis and intimal hyperplasia, including treating obstructed coronary artery and including applications of arteriovenous hemodialysis grafts in *in vivo* models.

The generic disclosure states that the present invention provides methods of introducing therapeutic agent capable of degrading collagen and/or elastin for facilitating reopening of biological conduit including dialating of the biological conduit (page 10, lines 8-14) and that therapeutic agent(s) include collagenase and/or elastase (page 12, lines 1-13). However, the generic disclosure also states that in some specific embodiments the degradation of elastin is not desirable and that collagenase is employed for preservation of elastic properties of conduit walls

(page 13, lines 10-15). The generic description as-filed does not recognize what specific embodiments or specific diseases and disorders might be treated with elastase. No dosages for applications of elastase are disclosed for treating biological conduits in *in vivo* applications. No dosages of elastase are disclosed for enlargement of the diameter of arteries and veins *in vivo* applications.

The exemplified disclosure of the *in vivo* applications is mostly related to treating dogs having stricture of common bile duct wherein the sole treating agent is collagenase only. There are two examples relating to measuring luminal diameters in dog models affected by stenosis due to intimal hyperplasia (pages 22-24) wherein the sole enzymatic agent is collagenase only. However, the results of assessments are not disclosed. Moreover, the elastase was not used at all in the exemplified disclosure.

Thus, there is no support for the newly inserted limitation drawn to administering "elastase in a dose sufficient to cause enlargement of the diameter of artery or vein" in the method of claim 25 because "dose sufficient" as intended for *in vivo* applications is not described in the as-filed specification. The "dose sufficient" of elastase is not described for mammal patients including human patients (claim 25 as amended and new claims 40-44). The "dose sufficient" of elastase is not described for treating artery and veins obstructed by stenosis (new claims 45-47). The "dose sufficient" of elastase is not described for treating artery and veins obstructed by intimal hyperplasia (new claim 48). The "dose sufficient" of elastase is not described for treating obstructed coronary artery in patient in need thereof (new claim 49). The "dose sufficient" of elastase is not described for *in vivo* applications of arteriovenous hemodialysis grafts (new claims 50-50-54).

This is a matter of written description, not a question of what one of skill in the art would or would not have known. The material within the four corners of the as-filed specification must lead to the generic concept. If it does not, the material is new matter. Declarations and new references cannot demonstrate the possession of a concept after the fact. Thus, the insertion of limitation drawn to administering "elastase in a dose sufficient to cause enlargement of the diameter of artery or vein" in the method for *in vivo* applications is considered to be the insertion of new matter for the above reasons.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 25 and 40-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kalles et al. ("Elastase-Induced Aneurysms in Rabbits: A Dose-Escalation Study". American Journal of Neuroradiology. February 2002, Vol. 23, No. 2, pages 295-298) and US 5,834,449 (Thomspson et al.).

Claims are directed to a method for enlarging the diameter of an artery or vein by locally administering to wall of the artery or vein in the human subject a composition with elastase in a dose sufficient to cause enlargement of the diameter of the artery or vein. Some claims are further drawn to the use of pancreatic elastase and to devices for elastase delivery including catheter. Some claims are further drawn to enlarging the diameter of arteries or veins including

coronary artery that are obstructed as result of stenosis, intimal hyperplasia and/or applications arteriovenous hemodialysis grafts.

Both cited reference by Kalles et al. and US 5,834,449 (Thomspson et al.) teach animal models of elastase-induced aneurysm that is dilatation or enlargement of blood vessels due to wall degeneration.

In particular, the reference by Kalles et al. describes a method for enlarging the diameter of an artery by locally administering to wall of the artery a composition with elastase in a dose sufficient to cause enlargement of the diameter of the artery (see entire document including Fig. 1). The reference teaches that degree of enlargement depends on both elastase concentration and duration of elastase exposure. The exemplified animal model is rabbit. However, the reference teaches similarity with other mammalian and human applications (page 295 at introduction).

In particular, US 5,834,449 (Thomspson et al.) also discloses a method for enlarging the diameter of abdominal aorta by locally administering porcine pancreatic elastase (col. 8, lines 50-65). Elastase is delivered by perfusion and, thus, with catheter.

Thus, both cited documents clearly teach enlargement of diameter of blood vessels as result of elastase administration. Although the model animals do not appear to have blood vessel obstructed as result of stenosis, intimal hyperplasia and/or applications arteriovenous hemodialysis grafts, these obstructed blood vessels are reasonably expected to be enlarged upon elastase treatment at least to some degree since elastase treatment lead to degeneration of blood vessel wall and dilatation. Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to administer elastase to the obstructed artery or vein of within the meaning of the instant invention with a reasonable expectation of success in

enlarging diameter of the artery or vein. Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1651

December 9, 2005

/V. Afremova/

VERA AFREMOVA

PRIMARY EXAMINER